

We claim:

1. A method of transdifferentiating an epidermal basal cell into cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, comprising:

5 culturing a proliferating epidermal basal cell population comprising one or more epidermal basal cell(s), said cell(s) derived from the skin of a mammalian subject;

exposing the cell(s) to an amount of an antagonist of bone morphogenetic protein (BMP) effective to antagonize endogenous BMP signal transduction activity; and

10 growing the cell(s) in the presence of at least one antisense oligonucleotide comprising a segment of a human MSX1 gene and/or a segment of a human HES1 gene, or homologous non-human counterpart of either of these, in an amount effective to suppress the expression of functional gene product of MSX1 or HES1, whereby the cell is transdifferentiated into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell.

2. The method of Claim 1, wherein the subject is a human.

3. The method of Claim 1, wherein the epidermal basal cell(s) is derived from a skin biopsy.

4. The method of Claim 1, wherein culturing the proliferating epidermal basal cell population further comprises separating keratinized epidermal cells from the epidermal basal cells in a calcium-free medium.

5. The method of Claim 1, wherein the amount of the antagonist of bone morphogenetic protein is about 10^{-6} to 10^{-4} M.

7. The method of Claim 1, wherein the antagonist of bone morphogenetic protein (BMP) is fetuin, noggin, chordin, gremlin, or follistatin.

8. The method of Claim 7, wherein the fetuin is mammalian or avian fetuin.

9. The method of Claim 8, wherein the mammalian fetuin is human, bovine, porcine, ovine, or equine fetuin.

10. The method of Claim 1, wherein the antisense oligonucleotide(s) is modified with one or more thio groups.

11. The method of Claim 1, wherein the amount of the antisense oligonucleotide is about 5×10^{-6} M to about 10^{-5} M.

12. The method of Claim 1, wherein the physiological and/or immunological feature is expression of a marker selected from the group consisting of nestin, neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2, glial fibrillary acidic protein (GFAP), O4, or a combination of any of these.

13. The method of Claim 1, wherein the morphological feature comprises one or more morphological neurite-like process(es) at least about 50 micrometers in length.

14. The method of Claim 1, further comprising growing the transdifferentiated cell in a

16. The method of Claim 14, wherein the neurotrophin is brain-derived neurotrophic factor (BDNF), ciliary neurotrophic factor (CNTF), platelet-derived growth factor (PDGF), nerve growth factor (NGF), neurotrophin (NT)-3, neurotrophin (NT)-4, or sonic hedgehog, and/or functional fragments of any of these.

sub F2
17. A transdifferentiated cell of epidermal origin having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell produced by the method of Claim 1.

18. The transdifferentiated cell of Claim 17, wherein the physiological and/or morphological feature is expression of a marker selected from the group consisting of nestin, neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2, glial fibrillary acidic protein (GFAP), O4, or a combination of any of these.

SUB D2
19. The transdifferentiated cell of Claim 17, wherein the cell exhibits a lack of mitotic activity under cell culture conditions which induce differentiation in neural progenitor cells.

20. The cell of Claim 17, wherein the transdifferentiated cell has a morphological, physiological and/or immunological feature specific to a neuronal cell.

21. The transdifferentiated cell of Claim 20, wherein the physiological and/or immunological feature is expression of neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2.

sub F3
22. The transdifferentiated cell of Claim 20, wherein the cell is a GABAergic cell.

23. The transdifferentiated cell of Claim 20, wherein the cell is a dopaminergic cell.

~~SUB D3 24. The transdifferentiated cell of Claim 17, wherein the morphological feature is one or more neurite-like process(es) at least about 50 micrometers in length.~~

25. The cell of Claim 17, wherein the transdifferentiated cell has a morphological, physiological, or immunological feature specific to an astroglial or oligodendroglial cell.

~~SUB D 26. The transdifferentiated cell of Claim 25, wherein the immunological feature is expression of glial fibrillary acidic protein (GFAP) or O4.~~

27. The transdifferentiated cell of Claim 17, wherein the cell is of human origin.

~~SUB D4 28. A cell culture derived from the transdifferentiated cell of Claim 17, comprising a plurality of cells that express one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell.~~

~~SUB DS 29. A transdifferentiated cell of epidermal origin, comprising a cell of epidermal basal cell origin, said transdifferentiated cell displaying one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, wherein the physiological and/or immunological feature is expression of a marker selected from the group consisting of nestin, 5 neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2, glial fibrillary acidic protein (GFAP), O4, or a combination of any of these.~~

30. The transdifferentiated cell of Claim 29, wherein the cell further displays the physiological feature of a lack of mitotic activity under cell culture conditions which induce differentiation in neural progenitor cells.

SUB D 32. The transdifferentiated cell of Claim 31, wherein the physiological and/or immunological feature is expression of neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2.

SUB F5 33. The transdifferentiated cell of Claim 31, wherein the cell is a GABAergic cell.

34. The transdifferentiated cell of Claim 31, wherein the cell is a dopaminergic cell.

SUB D 35. The transdifferentiated cell of Claim 29, wherein the morphological feature is one or more neurite-like process(es) at least about 50 micrometers in length.

36. The transdifferentiated cell of Claim 29, wherein the cell is of human origin.

37. The cell of Claim 29, wherein the transdifferentiated cell has a morphological, physiological, or immunological feature specific to an astroglial or oligodendroglial cell.

SUB D 38. The transdifferentiated cell of Claim 37, wherein the physiological and/or immunological feature is expression of glial fibrillary acidic protein (GFAP) or O4.

SUB F6 39. A cell culture derived from the transdifferentiated cell of Claim 29, comprising a plurality of cells that express one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell.

40. A method of using cells transdifferentiated from epidermal basal cells to identify a novel nerve growth factor comprising:

(a) transdifferentiating a population of epidermal basal cells into neuronal progenitor, neuronal, or glial cells by the method of Claim 1;

5 (b) culturing the transdifferentiated cells;

- (c) exposing the cultured cells, in vitro, to a potential nerve growth factor; and
- (d) detecting the presence or absence of an effect of the potential nerve growth factor on the survival of the cells or on a morphological or electrophysiological characteristic and/or molecular biological property of said cells, whereby the presence of an effect altering cell survival, a
- 10 morphological or electrophysiological characteristic and/or a molecular biological property of the cells indicates the activity of the novel nerve growth factor.

41. A method of using cells transdifferentiated from epidermal basal cells to identify a potential chemotherapeutic agent comprising:

- (a) transdifferentiating a population of epidermal basal cells into neuronal progenitor, neuronal, or glial cells by the method of Claim 1;
- 5 (b) culturing the transdifferentiated cells;
- (c) exposing the cultured cells, in vitro, to a potential chemotherapeutic agent; and
- (d) detecting the presence or absence of an effect of the potential nerve growth factor on the survival of the cells or on a morphological or electrophysiological characteristic and/or molecular biological property of said cells, whereby the presence of an effect altering cell survival,
- 10 a morphological or electrophysiological characteristic and/or a molecular biological property of the cells indicates the activity of the chemotherapeutic agent.

42. A method of using transdifferentiated cells to screen a potential chemotherapeutic agent to treat a nervous system disorder of genetic origin, comprising:

- (a) transdifferentiating epidermal basal cells derived from a human subject having a genetically-based nervous system disorder to a population of neuronal cells by the method of
- 5 Claim 1;

(b) culturing the transdifferentiated cells;

(c) exposing the cells, in vitro, to a potential chemotherapeutic agent; and

(d) detecting the presence or absence of an effect of the potential nerve growth factor on the survival of the cells or on a morphological or electrophysiological characteristic and/or

10 a morphological or electrophysiological characteristic and/or a molecular biological property of the cells indicates the activity of the chemotherapeutic agent.

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43. A kit for transdifferentiating an epidermal basal cell into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, comprising:

(A) an antagonist of bone morphogenetic protein (BMP); and

(B) at least one antisense oligonucleotide comprising a segment of a human MSX1 gene, a segment of a human HES1 gene, or a non-human homologous counterpart of either of these.

44. The kit of Claim 43, further comprising instructions for using (A) and (B) in transdifferentiating a subject's epidermal basal cell(s).

45. The kit of Claim 43, wherein the antagonist of bone morphogenetic protein (BMP) is fetuin, noggin, chordin, gremlin, or follistatin.

46. The kit of Claim 43, further comprising a retinoid compound and, optionally a nerve growth factor or neurotrophin.

47. The kit of Claim 46, wherein the retinoid compound is all-trans retinoic acid or Vitamin A.

48. The kit of Claim 46, wherein the neurotrophin is brain-derived neurotrophic factor (BDNF), ciliary neurotrophic factor (CNTF), platelet-derived growth factor (PDGF), nerve growth factor (NGF), neurotrophin (NT)-3, neurotrophin (NT)-4, sonic hedgehog, and/or functional fragments of any of these.